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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,346	07/20/2001	Lance E. Steward	D-2885CIP	2952

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/910,346	STEWARD ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29,30 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29,30 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/19/04 & 2/28/02 2/28/03*
4) ☐ Interview Summary (PTO-413) Paper No(s). ____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *WO98/08540.*

DETAILED ACTION

Sequence Rules

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application still fails to comply with the requirements of 37 CFR 1.821 through 1.825 because 37 CFR 1.821 (a)(2)(c-d) states that *each sequence disclosed must appear separately* in the Sequence listing and *in the text of the description* and claims whenever described. In other words, Applicants are not fully responsive to communication 20040519. Pages 16 & 20 (i.e., as it relates to Figure 3) must be amended to indicate the appropriate SEQ ID NOs.

Note that failure to respond to both the requirements for sequence compliance and the restriction requirement below will be held as *nonresponsive*, and may result in *abandonment* of this application.

Election/Restrictions

2. Applicant's election with traverse of Group IV (claims 29-30 & 33, as it relates to botulinum toxin B in the reply filed on 3/09/04 is acknowledged. The traversal is on the ground(s) that "it is not undue burden for the Office to search for whether SEQ ID NO:23 has been added to any wild-type botulinum toxins. For example, ... botulinum toxins types A through G are readily accessible through public data bases". This is not found persuasive because each of these different botulinum toxins are structurally unique and possess their own unique functional properties; thereby, making a search of any "neurotoxin" an undue burden, and for the reason made of record. The requirement is still deemed proper and is therefore made FINAL.

Claims directed to any different modified neurotoxin are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/09/04. It is noted that the amended claims are now directed toward only modified botulinum toxin B.

Information Disclosure Statement

3. The information disclosure statements filed 2/28/02, 2/28/03 & 7/19/04 fail to fully comply with 37 CFR 1.98(a)(2), which requires a *legible copy* of each U.S. and foreign patent; each *publication* or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered, for those references crossed-out.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-30 & 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific modified BoNT/B neurotoxin proteins with a definable sequence change and recited definable and assayable function, does not reasonably provide enablement for any functionally uncharacterized modified BoNT/B molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

For example, pages 7-8, 11, 13-14, 34 & 52 of the specification disclose that modified neurotoxins can increase biological half-life, or increase their biological activity. Specific examples of increased biological activity include reducing or inhibiting exocytosis of neurotransmitters from a presynaptic neuron, or alleviating inflammatory pain. The problem is that is unknown what specific function is envisioned that a "modified" BoTx/B neurotoxin is expected to possess (i.e., especially as it relates to unknown modified BoTx/B neurotoxins comprising an [*additional*] tyrosine-based motif of SEQ ID NO:23), in order to enable the claimed modified BoTx/B neurotoxins; thereby, preventing the skilled artisan from knowing how to make and use the currently claimed modified BoTX/B neurotoxins, without requiring undue experimentation to determine such. It is suggested that amending the claims to recite a distinguishable and assayable function, such as increased half-life may obviate this rejection.

5. Claims 29-30 & 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is ambiguous whether an "additional" tyrosine-based motif is added to the claimed BoTN/B molecule to make it a "modified" BoTx/B, which alternatively still contains its naturally-occurring tyrosine based motifs, or whether the BoTx/B is modified at different amino acid residues.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29-30 & 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams et al/ Ophidian Pharm Inc (WO 9808540 A1).

Williams et al teach a histidine-tagged fragments of botulinum toxin type B (i,e. a "modified botulinum toxin/B of 472 amino acid residues, versus 1291 amino acid residues in wildtype botulinum B toxin; pgs 300-305 & Example 35; as it relates to claim 29), in which a leucine residue is present as the hydrophobic residue in position #4 of SEQ ID NO:23 at positions #s: 293 & 350 of both the Eklund 17B strain fragment, and the Danish strain fragment (i.e., as it relates to claims 30 & 33). See attachment at end of reference for sequence comparison.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961. The fax phone number for this Group is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert C. Hayes, Ph.D.
September 16, 2004

ROBERT C. HAYES, PH.D.
PATENT EXAMINER